

CASE REPORT

BLUE RUBBER BLEB NEVUS SYNDROME

Daleth Rodrigues, Maria Lucia de Moraes Bourroul, Ana Paula Scoleze Ferrer, Henrique Monteiro Neto, Manoel Ernesto P. Gonçalves and Silvia Regina Cardoso

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SUMMARY: The blue rubber nevus syndrome consists of multiple venous malformations in the skin and gastrointestinal tract associated with intestinal hemorrhage and iron deficiency anemia. Other organs may be involved. The causes of this syndrome are unknown. Its most common presentation is in the form of sporadic cases, but dominant autosomal inheritance has been described. It is a condition that affects both sexes equally, and its occurrence is rare in the black race.

We present a case of this syndrome diagnosed in a 11-year-old patient. He had severe anemia and a venous swelling on the trunk. Similar lesions were found in the stomach, bowel, and on his foot.

We emphasize the main clinical aspects: intestine, eyes, nasopharynx, parotids, lungs, liver, spleen, heart, brain, pleura, peritoneum, pericardium, skeletal muscles, bladder, and penis lesions, systemic complications that may occur to these patients which are thrombosis and calcification, as well as consumptive coagulopathy and thrombocytopenia that may occur within the nevi.

DESCRIPTORS: Blue rubber bleb nevus syndrome. Hemorrhage. Anemia. Vascular malformations.

The blue rubber bleb nevus syndrome was probably first observed by Gascoyen in 1860. He described a congenital parotid lesion in an adult who died by suffocation after considerable tumor growth. The patient presented several nevi in the skin, and the necropsy revealed similar lesions on the intestinal surface¹⁻⁵.

In 1958, almost a century later, William Bennet Bean described a condition with similar findings: vascular nevi of the skin, gastrointestinal tract hemangiomas, and hemorrhage, leading to iron deficiency anemia. He gave this particular association the name of “blue rubber bleb syndrome” due to the bluish color of the nevi, and to their rubbery consistency at palpation²⁻⁷.

The typical finding in this disease

is venous malformations, that are present at birth or in the first years of life. They are bluish lesions that range from a few millimeters to several centimeters in diameter and that occur preferentially in the trunk and upper extremities. Vascular malformations of the gastrointestinal tract are part of the syndrome, and in most cases lead to extensive hemorrhages with hematemesis, melena, or rectal bleeding. At other times, they cause occult and chronic bleeding, manifested by iron deficiency anemia^{4,5,7}.

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From the Children's Institute, Hospital das Clínicas, Faculty of Medicine, University of São Paulo.

unknown. Its most common presentation is in the form of sporadic cases, but dominant autosomal inheritance has been described. It is a condition that affects both sexes equally, and its occurrence is rare in the black race^{1,8,9}.

Since Bean's description of the syndrome, less than 150 cases have been reported in the literature. We describe here a case of the blue rubber bleb nevus syndrome in an adolescent who sought medical assistance due to extreme pallor for several months.

Early detection of this condition is important because it alerts the physician to the possibility of associated bleeding, anemia, and other systemic complications that may occur, in addition to the genetic counseling that can be instituted after the diagnosis^{1,7}.



Figure 1 - Cistic lesions on the left supraclavicular area.



Figure 2 - Vascular nodule on the right sole.

CASE REPORT

S.A. A., male, brown-skinned, born in the State of Alagoas, Brazil, living in the City of São Paulo for the past five months, fifth child of a non-consanguineous couple, sought the Emergency Service of the Children's Institute of the Clinics' Hospital of the Fac-

ulty of Medicine of São Paulo University, due to cutaneous pallor "for the past 3 months" and a growing cystic mass in the left supraclavicular region, present since birth, but that had recently been increasing in size. The patient had a history of removal of "cysts" in that part of the body, at 2 months and again at 2 years of age,

with the mass always reappearing in the same place. No surgical pathology results were available from the previous surgeries. One year earlier, the child had been treated for schistosomiasis, without controls after treatment. The patient did not report any type of bleeding, loss of weight, jaundice, fatigue, or fever. There was no

family history of the disease. It was not possible to get precise information about previous food intake, but the current nourishment provided to the child was adequate.

At the physical examination, the boy was found to be in good general condition, extremely pale, hydrated, eupneic, tachycardiac, and without visceromegalies. The examination revealed 5 cystic, varicose, bluish, pressoreceptive formations in the left supraclavicular region, with diameters that varied between 2 and 6 cm, and that immediately returned to their original form after digital pressure (Fig. 1). The child also presented a nodule of 2 cm of diameter at the sole of the left foot, in which small caliber vases could be visualized, and another of similar characteristics in the first left toe (Fig. 2).

The admission hemogram revealed: Hb = 4.2 mg/dL, Ht = 15%, VCM = 50, HCM = 14, CHCM = 28, anisocytosis, microcytosis and macrocytosis, hypochromia, poikilocytosis, and tear-shaped ovalocytes and erythrocytes. The leukocyte and platelet counts were normal. Before receiving a transfusion of erythrocyte concentrate, blood samples were collected for etiologic analysis of the anemia that showed 12 mcg/dL of iron, 6.5 mcg/L of ferritin, total iron-binding capability of 525 mcg/dL, and normal hemoglobin electrophoresis and globular resistance curve.

The Doppler ultrasound examination of the left supraclavicular region showed a mass in the soft tissues of heterogeneous texture, with small anechoic areas, suggesting the presence of liquid. The Doppler image revealed that there was discreet flow and vascularization within the mass.

The diagnostic search for a clinical condition presenting the association of vascular malformations with serious iron deficiency anemia led the authors

to consider the blue rubber bleb nevus syndrome and thus to initiate the search for vascular malformations in the gastrointestinal tract by collecting of two samples for the investigation of occult blood in the feces. Both specimens were positive. In view of the confirmation of intestinal bleeding, endoscopic exams were then performed.

The colonoscopy showed wine-colored vascular lesions of about 0.6 cm in the rectum, sigmoid, descendent, and transverse colon, with raised, irregular surfaces, which were brittle to the contact with the equipment. In the cecum, near the ileo-cecal valve there was another larger lesion, measuring approximately two cm at its widest diameter.

The upper gastrointestinal endoscopy revealed three small wine-colored lesions in the stomach and a larger one in the anterosuperior duodenal wall, measuring two cm at its widest diameter.

The investigation of systemic involvement was completed with an abdominal ultrasound exam, contrasted cranium tomography, eyeground examination and test for consumptive coagulopathy (prothrombin time, total activated thromboplastin time, fibrinogen dosage and D-dimer), all of which yielded normal findings. The karyotype collected after consultation with the geneticist also showed a normal result (46 XY).

Endoscopic sclerotherapy of the gastric lesions was initiated and was later also performed in the colon lesions, yielding good results.

The child was kept on iron replacement therapy by mouth and proceeded to show hematimetric rates within normal levels for his age and sex.

To avoid the eventual risks involved in transfusions of blood derivatives, the patient was vaccinated against type B hepatitis.

DISCUSSION

The blue rubber bleb nevus syndrome is a rare condition in which cutaneous vascular malformations are associated with gastrointestinal hemorrhage due to the presence of similar lesions in the gastrointestinal tract.¹ Although the literature often denominates these lesions as "hemangiomas", they are really vascular malformations with regard to their histological characteristics. Hemangiomas have diverse characteristics including hyperplastic endothelium, while the vascular malformations were coated by normal endothelium. In children, hemangiomas tend to grow considerably during the first 6 months of life, moderately in the second semester, and decrease in size, from 12 months of age on, and 95% of them will have disappeared by the time the child reaches 10 years of age. Vascular malformations do not usually present this behavior¹⁰.

In the blue rubber bleb nevus syndrome, intestinal lesions are more frequent in the small intestine, although any anatomical site, from the mouth to the anus, may be affected. When the colon is affected, they are more frequent in the rectal or distal areas⁹. Other sites may also be affected, such as the eyes, nasopharynx, parotids, lungs, liver, spleen, heart, brain, pleura, peritoneum, pericardium, skeletal muscles, bladder, and penis^{1,2,5,7}. Waybright correlated venous malformations in the sublingual region with similar lesions in the central nervous system. Orthopedic abnormalities, such as bone deformities and hypertrophy, fractures, and articular involvement may also be present^{1,2,5,7}. The patient reported here showed venous malformations in the skin (trunk and feet), stomach, duodenum, and colon. There were no sublingual lesions or orthopedic alterations.

In this pathology, the appearance, number, size, and distribution of the lesions may vary. The largest lesion found in our patient was in the trunk, which has been described as a preferential site of occurrence^{1,10}.

The nevi are often present in early childhood, and they may grow, increase in number, and lead to complications^{3,8}. Some patients report painful lesions, which may be due to the contraction of surrounding smooth muscles^{1,3,5,7}. There are also descriptions of lesions that cause increased sweating, possibly due to the proximity of the nevi to sweat-secreting glands^{1,3,7}. Our patient presented lesions first seen at birth that had been increasing in size, but that never caused local pain or excessive sweating. His major complaints regarded the inconvenience that was related to aesthetics. The reappearance of the lesions after surgical removal, as occurred in this case, has been described in the literature, but their evolution to malignancy has never yet been reported^{1,5,9}.

Thrombosis and calcification, as well as consumptive coagulopathy and thrombocytopenia, may occur within the nevi^{1,6,11}, but none of these were found in the patient described here.

This syndrome has been detected in successive generations, but that is not its most common presentation. Some authors believe that its transmission is predominantly autosomal^{1-3,7}. We could not identify any similar cases among our patient's relatives. The child's mother had presented hematemesis 1 year before the initial consultation, but high digestive endoscopy revealed a gastric ulcer. The patient's 6 brothers are healthy, and his father died in a car crash.

The main consequence of skin hemangiomas is aesthetic, since they hardly ever bleed. Surgical excision of the cutaneous lesions is limited to those that occur in areas of higher risk of trauma, as in our patient, for whom surgery was indicated for the lesions in

the sole of the foot. The treatment may be by surgery, by local or systemic corticotherapy, or by laser photocoagulation^{5,7,10,12}.

The intestinal nevi, in contrast to the cutaneous nevi, are easily injured and can bleed profusely. The bleeding may be massive, requiring transfusion or surgery. The bleeding may also be occult, and when it is chronic, it may lead to iron deficiency anemia^{1,7}. Our patient never presented any visible bleeding, but he certainly suffered chronic blood losses, as indicated by the several nevi found in his gastrointestinal tract. Symptoms of intestinal obstruction may occur due to intussusception, secondary to an angiomatous intestinal involvement^{1,9,11}. We chose to perform the endoscopic exams of the gastrointestinal tract directly because they are the most reliable diagnostic means to detect these lesions. Additionally, in certain situations, endoscopic exams can act therapeutically owing to the sclerosis of the localized lesions⁷.

Treatment of gastrointestinal lesions varies according to their extent, localization, and consequences. For patients with small numbers of lesions or with lesions that are too diffuse and having anemia without open bleeding, elective transfusions and iron replacement have been recommended. For more significant hemorrhages, surgical resection, endoscopic sclerosis, laser photocoagulation, and therapy with interferon have been proposed^{1,5-7,9}. The management of these patients requires continued follow-up by outpatient consultations, in which new intercurrent diseases are evaluated and periodical monitoring of hematimetric rates is performed.

The blue rubber bleb nevus syndrome must be differentiated from inherited hemorrhagic telangiectasia (Rendu-Osler-Weber Syndrome). These patients may present palindromic epistaxis at the beginning of life

and present telangiectasias in the adolescence. In this condition, the gastrointestinal lesions are similar, but the skin lesions are morphologically and histologically different. They are punctiform, red-bluish, and never reach the dimensions of those of the blue rubber bleb nevus syndrome. They affect the mucosa, lips, face, trunk, lungs, intestines, fingers, and lower limbs, but the sublingual lesions are very suggestive^{3,7,9}.

The Klippel-Trenaunay Syndrome presents varicosities, hypertrophy, and soft tissue and bone deformities, as well as "port wine nevus", generally located in just one of the extremities. It is also possible to find arteriovenous fistulas^{3,4,7,9,10}.

The Maffucci Syndrome is characterized by diffuse vascular malformations in the skin and soft tissues, associated with bone malformations and chondrodysplasias. Gastrointestinal tract lesions do not occur^{3,7,9,10}.

There are other conditions in which vascular skin lesions are associated with lesions in other organs, such as meninges, in the Sturge-Weber Syndrome; brain and retina, in the Von-Hippel-Lindau Syndrome; and spinal cord, in the Cobb Syndrome and others^{3,7}.

CONCLUSION

The presentation of this case emphasizes the importance of an integrated approach in which personal and family history, habits, lifestyle and physical evaluation are associated and made compatible. In this case, since the severe iron deficiency anemia did not seem to be a result of the previous alimentary history, the search for a pathology that could associate the findings of the physical exam was essential to arrive at the diagnosis.

As it was stated in the Discussion, there are several clinical conditions in

which vascular skin lesions are associated with similar ones in other organs, as well as with other systemic alterations or specific complications, such

as anemia, consumptive coagulopathy, intestinal obstruction, bone deformities, ocular and central nervous system alterations. Thus, the early detection of

specific situations becomes essential as much for treatment as for genetic counseling.

RESUMO

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RODRIGUES D e col. - Síndrome de “nevo em bolha de borracha azul”. **Rev. Hosp. Clín. Fac. Med. S. Paulo** 55 (1):29-34, 2000.

A síndrome do nevo em bolha de borracha azul “blue rubber bled nevus syndrome” é caracterizada por malformações venosas da pele e trato gastrointestinal, associadas a hemorragia intestinal e anemia ferropriva. Outros órgãos podem estar envolvidos. As causas desta síndrome são desconhecidas e sua apresentação

mais comum é na forma de casos esporádicos, mas herança autossômica dominante já foi descrita. É uma condição que afeta igualmente ambos os sexos e sua ocorrência é rara na raça negra.

Apresentamos um caso desta síndrome diagnosticada em criança de onze anos de idade. Ela apresenta anemia grave e tumorção venosa do tronco. Lesões semelhantes foram encontradas no estômago, intestino e um dos pés. São enfatizados os aspectos clínicos principais – lesões no

intestino, olhos, nasofaringe, parótida, pulmões, fígado, baço, coração, cérebro, pleura, peritônio, pericárdio, músculo esquelético, bexiga e pênis – e complicações sistêmicas que podem ocorrer nestes pacientes – trombose e calcificação dos nevus, assim como coagulopatia de consumo e trombocitopenia.

DESCRITORES: Síndrome do nevo em bolha de borracha azul. Hemorragia. Anemia. Malformações venosas.

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